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2. ~~Patent application number~~
(The Patent Office will fill in this part)

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   University of Wales, Bangor, College Road, Bangor, Gwynedd L57 2DG

   Patents ADP number *(if you know it)* — 07967319001

   If the applicant is a corporate body, give the country/state of its incorporation — United Kingdom

4. Title of the invention

   TRAVELLING WAVE DIELECTROPHORETIC APPARATUS AND METHOD

5. Name of your agent *(if you have one)* — GALLAFENT & CO

   "Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)* — 9 STAPLE INN
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TRAVELLING WAVE DIELECTROPHORETIC APPARATUS AND METHOD

This invention relates to an apparatus and method of using the technique of dielectrophoresis, and relates particularly to an arrangement for concentrating or diluting or transporting or separating or detecting or characterising particles.

The technique of dielectrophoresis (DEP) is described in the book "Nanotechnology in Medicine and the Biosciences", Ed RRH Combs and D W Robinson, published by Gordon & Breach, Amsterdam, chapter 11 by Ronald Pethig, especially pages 153 to 168. Dielectrophoresis is the movement of particles in non-uniform electric fields. Unlike electrophoresis, charges on the particle itself are not necessary for the effect to occur and AC rather than DC fields are employed.

When an electric field is applied to a system consisting of particles suspended in a liquid medium, a dipole moment is usually induced in each particle as a result of electrical polarisations forming at the interfaces that define their structure. If the field is non-uniform, the particles experience a translational force, known as a dielectrophoretic force, of magnitude and

polarity dependent on the electrical properties of the particles and their surrounding medium. This force is also a function of the magnitude and frequency of the applied electric field.

In a paper by Kaler et al, Biophys. J., Volume 63, July 1992, pages 58 to 69, signals of different frequencies are applied to a single pin electrode so that a particle simultaneously experiences positive and negative DEP forces; such an arrangement can be used to characterise particles, but not separate them. Conventional DEP is used with static fields.

Another application of the technique of DEP is described in WO 98/04355, British Technology Group, in which a particle-containing liquid is caused to flow over a comb-like array of electrodes to which signals at different frequencies are applied; particles of different characteristics are urged preferentially towards or away from different DEP regions of the array, so that the particles can be characterised. A flowing fluid and conventional DEP with static field are used.

The technique of travelling wave DEP is also described by Pethig, chapter 11, pages 161 to 165. Signals at different phases are applied to a spaced array of electrodes so as to produce a travelling electric field. It is explained by Pethig, with due reference to the work of others in the field, in particular Y Huang et al "Electrokinetic behaviour of colloidal particles in travelling electric fields: studies using yeast", J. Phys D: Appl. Phys., 26, pages 1528 to 1535, 1993, that in order for travelling wave DEP (TWD) to occur in a travelling field, the particle must experience a negative DEP force, pushing it away from the electrodes and thus levitating it above them. There must also be an imaginary component to the DEP force for TWD to

occur, so that the particle will experience a translational movement in the field. The frequency range over which TWD is possible is indicated as TW in Figure 1 which illustrates the principle of conventional TWD at a single frequency on a single particle type. TW can be considered as the travelling wave window for the particle. Within this window the particle will travel at different speeds dependant upon the level of the imaginary component of the force I, as well as the levitation height of the particle that results from the real part of the force R. The profile of the travelling speed for a particle within the travelling wave window is referred to as the travelling wave "envelope".

Throughout this specification, the term "particle" is used to include biological cells, bacteria, viruses, parasitic microorganisms, DNA, proteins, biopolymers, non-biological particles, or any other particle which may be suspended in a liquid, in which a dielectrophoretic force can be induced. It also applies to chemical compounds or gases dissolved or suspended in a liquid, where a dielectrophoretic force can be induced.

According to the invention, a method of travelling wave dielectrophoresis comprises applying to a suspension of particles a first signal at a first frequency and at a plurality of different phases whereby the particles experience a travelling wave dielectrophoretic force, and simultaneously applying a second signal at a second frequency whereby either the real part or the imaginary part of the travelling wave dielectrophoretic force on the particles at the first frequency is altered in magnitude.

In one arrangement, the second frequency is selected so that the range of frequencies delimiting the travelling

wave window (as defined above) of the particles is made narrower or wider. The second frequency can be selected to generate a stationary DEP field which is either positive or negative, a TWD field with the imaginary part of the force equal to zero, or a TWD field with the real part of the force equal to zero.

Alternatively, the second frequency is selected so that the levitation height of the particles above electrodes applying the dielectrophoretic force is varied. The second frequency can be selected to generate a stationary DEP field which is either positive or negative, or a TWD field with the imaginary part of the force equal to zero.

In another arrangement, the second frequency is selected so that two particle types travel simultaneously, the particle types being such that only one type would travel on application of the first frequency.

In another arrangement, the second frequency is selected so that of two particle types, one type is held by the electrodes, while the other type travels, the particle types being such that both types would travel on application of the first frequency.

In another arrangement, the second frequency is selected so that the relative travelling speeds of two different particle types is increased, usually by applying a second frequency such that one particle type experiences a significant imaginary component of the TWD force.

Optionally, a third frequency may be applied to achieve the required effect, the third frequency also being such as to generate a static or TWD field.

In another arrangement, the second frequency is selected

so that particle types travel in opposite directions which, on application of the first frequency only, would travel in the same direction. The second frequency preferably generates a TWD field having strong real and imaginary components, and it is highly likely that a third frequency will be applied to achieve the required result.

In all arrangements, a third or more particle types may be present, and a third or more frequencies may be applied.

The invention will now be described by way of example only with reference to the accompanying drawings in which:

Figure 2 illustrates five possible additional second frequencies.

Figure 3 illustrates the effect of increasing magnitudes of a selected second frequency on a single particle type.

Figure 4 illustrates the principal separation of two particle types by conventional TWD at a single frequency, and is a reference Figure.

Figure 5 illustrates the effect on the Figure 4 arrangement of additional travelling wave signals at double the magnitude.

Figure 6 is a reference Figure similar to Figure 4.

Figure 7 illustrates the effect of adding a second frequency F6 to the Figure 6 arrangement.

Figure 8 illustrates the effect of adding a third signal

to the Figure 6 arrangement.

Figure 9 shows schematically a TWD apparatus, and

Figure 10 illustrates a DEP spectrum for red blood cells.

In Figures 1 to 8, the expected dielectrophoretic response for the particles is shown, the particles being suspended in a medium of conductivity 2mS/cm.

In Figure 1, taken from the prior art, the effect on red blood cell (rbc) particles of the application of a dielectrophoretic field over a wide range of frequencies is shown. The real component R and the imaginary component I of the DEP force are plotted on an arbitrary scale against log frequency.

As is well-known, application of a static field is referred to as conventional DEP and only the real component of the DEP force is excited. With TWD, both the real and the imaginary components of the force are excited.

Consider now the effect of applying an additional signal at a second frequency. In Figure 2, the frequencies of five possible additional signals are shown by the arrows on the general dielectrophoresis spectrum; the Figure is a reference Figure, none of the frequencies F0 to F4 is applied to the spectrum.

At frequency F0, there is a high negative real part and no imaginary part.

At frequency F1, there is no real part and a high negative imaginary part.

At frequency F2, there is high positive real part, and no imaginary part.

At frequency F3, there is no real part, and a high positive imaginary part.

At frequency F4, there is a negative real part, and no imaginary part.

The effect of applying an additional signal at frequency F2 on the red blood cell (rbc) spectrum is shown in Figure 3. The signal is now indicated by a line to indicate actual application. The imaginary part I shown dotted is unchanged because at frequency F2, there is no imaginary component (I = 0), but the additional signal causes the real part R, which is positive at frequency F2, to becoming more positive accordingly to the amplitude of the signal F2, as shown by the chain dotted lines R', R", R'", etc. The increase in value is proportional to the square of the voltage of the applied signal F2.

As the amplitude of signal F2 increases, the real part R of the net DEP force becomes more positive R', R", R"'. The travelling wave window becomes narrower, as indicated by the arrow TW" corresponding to the real part R2". The particles therefore travel over narrower ranges of applied frequency, which results in increased selectivity and sensitivity to the control and characterisation of the particle.

Alternatively, by selection of the appropriate conditions, the TW window can be widened to decrease sensitivity. Referring to Figure 2, this could be achieved by applying a second signal at frequency F0.

In another variation, the levitation height of the

particles above the DEP electrodes can be varied. One way to achieve this, see Figure 2, is by applying a travelling field signal of frequency FO or F2, i.e. a signal where the real part of the DEP force is either positive or negative, and the imaginary part is zero, the levitation height of particles above the DEP electrodes can be varied.

Alternatively, a static DEP field can be used, i.e. one which induces only a real and no imaginary DEP component. Referring again to Figure 2, any frequency below F1 will apply a negative DEP force, thus increasing the levitation height of the particles above the electrodes. Similarly, any frequency between F1 and F3 will apply a positive DEP force, thus reducing the levitation height of the particles.

As a further variation for adjusting the levitation height of a particle, any frequency which has a real positive or negative component and additionally an imaginary component may be used. However, using such a frequency results in changing the imaginary component having a direct effect on the travelling speed of the particle, and so this is generally not preferred. Static DEP fields are preferred for varying the levitation height of particles above the DEP electrodes.

Controlling the levitation height of particles in a TWD field has several advantages. In the region very close to the electrodes, the DEP forces are their strongest, but there is considerable spatial variation of the field. Particles moving in this region of the field are seen to move non-evenly, and may become trapped. On the other hand, in regions significantly above the electrodes, the DEP forces are considerably reduced. There is, therefore, an optimum region within the field for particle movement. Being able to control particle

height within this field provides improved repeatability and separation efficiency. It also provides considerable benefit when TWD is combined with field flow fractionation (FFF).

Without use of this inventive arrangement, control of particle height is complex. For example, adjusting the voltage of the applied signal will alter the particle height, but will also directly change the translational movement of the particle as the imaginary component of the force is also changed. Changing the suspending medium conductivity or electrode geometry will also directly change the imaginary component. By use of the invention, the real or imaginary components may be changed individually, allowing control and versatility previously not attainable.

The inventive technique has a practical application in particle separation. Figure 4 shows the real and imaginary parts of the DEP spectra of red blood cells and E-coli bacteria. Inspection shows that the travelling wave window for both particles is similar, about 20 kHz to 600 kHz. In a conventional arrangement for separation of these two particle types, TWD would be applied at a frequency of about 200 kHz. A line F5 is shown on Figure 4 at this frequency; at 200 kHz, the E-coli cells experience much stronger levitational (negative real part R) and translational (imaginary part I) forces than the red blood cells, and would therefore be caused to move relatively rapidly in the TWD field while the blood cells would move relatively slowly. However, for effective separation, a very long TWD electrode array would be needed for efficient separation, particularly if high particle concentrations are employed.

In contrast, suppose that the difference in DEP

properties of the two particle types is magnified. This can be achieved by the application of a second frequency and reference Figure 4 indicates by the arrow F6 a possible value of this frequency. Figure 5 shows the effect on the spectra of applying an additional signal at frequency F6; the real component of the blood cells and the imaginary components of both cell types are positive at this frequency and therefore have been shifted upwards, while the real component of blood cells is negative at this frequency and has been shifted downwards. The effect of applying a second TWD frequency F5 is that the blood cells now experience a small positive DEP force and will be attracted to the electrodes and will not be levitated. The blood cells will therefore not travel in the TWD field. The E-coli cells will experience a negative DEP force and an imaginary component of the force, and will therefore travel in the TWD field. Effective particle separation is therefore possible because only one particle type travels.

The frequency F5 is a conventional travelling field signal applied at different phases, e.g. 0°, 90°, 180°, 270°, and at arbitrary equal amplitudes. The second frequency F6 is similarly a conventional travelling wave signal.

In a variation, the second frequency signal may be applied as a static field, e.g. at phases of 0° and 180°, which will affect the real component of the DEP spectrum, while the imaginary component remains unchanged.

In an important variation, the second signal may be applied as a travelling field of reversed polarity, which will change the polarity of the imaginary component of the DEP spectrum, with the real component

remaining unchanged.

Figure 6 is a reference figure similar to Figure 4; close inspection will show that frequency F7 in Figure 6 is slightly lower in value than F5 in Figure 4, and frequency F8 is slightly higher in value than F6 in Figure 4.

If the signal at frequency F8 is applied to achieve a DEP force of twice unity height, with reference to the spectra shown in Figure 6, the result is that illustrated in Figure 7. At frequency F8, the imaginary components for both blood and E-coli are positive and the real component for blood is positive, and therefore all increase in value. The real component of E-coli is negative and decreases in value. As shown in Figure 7, frequency F7, the TWD frequency, the effect is that the imaginary component for the blood cells has changed from a negative to a positive value, but the real component for blood is no longer negative, thus the blood cells do not levitate and TWD is not possible.

Consider now the application of a third signal at unity amplitude and frequency F9 (see Figure 6). The result is shown in Figure 8. At frequency F7, the effect of applying the three frequencies F7, F8 and F9 is that the real part of the net DEP force for both particles is negative, and that both particles have an imaginary component to their DEP force. The blood cells have a small negative imaginary component, while the E-coli have a positive imaginary component. The TWD conditions are therefore met for both particle types but the blood cells and E-coli will travel in opposite directions because their imaginary components are of different sign. Improved separation of the two particle types therefore results.

As a variation, a reverse phase travelling field signal may be used in the examples in Figures 5 to 8. A reverse phase travelling field signal is achieved, for example, by swapping the 90° and 270° relative phases of a quadrature phase signal. The effect of applying such a signal is to invert (i.e. reverse polarity, but same magnitude) the imaginary part of the dielectrophoretic force, while leaving the real part of the force unchanged; the translational TWD force resulting from the two fields are now in opposite directions.

Referring again to Figure 4, suppose frequency F6 is applied in reverse phase. The imaginary parts I for red blood cell (rbc) and E-coli forces would now be negative, while the real part of the force is negative for the E-coli and positive for rbc (i.e. the same as before). Using combinations of forward and reverse phase travelling fields and static fields, improved particle manipulation and separation can result.

In another variation, in certain conditions, the application of a travelling field can induce a significant hydrodynamic fluid movement, which is known. It has been found that by applying a second frequency signal to induce such hydrodynamic fluid movement in conjunction with a first frequency TWD signal, improved particle separation can result.

For example, suppose two particle types are to be separated, one type experiencing strong and the other relatively weak TWD translational movement; an example is E-coli and rbcs as shown in Figure 4. Applying frequency F5 and, in addition, applying a second frequency signal to induce hydrodynamic fluid movement in reverse direction and of specific magnitude such that the red blood cells may be moved predominantly by fluid flow, while the E-coli travel in the opposite direction

by TWD forces. A travelling field of 10 kHz can be used to induce such fluid movement. The second frequency travelling field signal will alter the magnitude of the real and/or imaginary components of the TWD forces on the particles, as well as additionally inducing the hydrodynamic fluid movement.

Applying travelling fields of two or more frequencies can therefore be used to separate particles by a combination of hydrodynamic and TWD forces, with the first frequency signal chosen to induce the desired TWD forces on the particles and the second frequency signal chosen to induce significant hydrodynamic fluid movement. Preferably, the travelling field signals to induce the combination of hydrodynamic and TWD forces is applied to the same TWD electrodes.

In Figure 9, a general apparatus for TWD is illustrated. A glass substrate 20 has on its upper surface an array 22 of parallel electrodes, each of which is connected by a multiple connector 24 to a signal generator 26. The substrate 20 can be covered by protective cover 28 (conveniently a second glass substrate), the substrates being separated by a spacer (not shown) to form a thin cell. A suitable spacer is a plastic strip.

The cell is illuminated from below by a light source 30, and is viewed from above by an optical microscope/video recorder 32 connected to a display screen 36.

In use, a suspension of particles in a liquid is placed on the substrate 20 and the cover 28 put into place. The signal generator 26 is arranged to apply signals of different phases to the electrodes in the array 22. For example, the signal generator 26 may be a four phase sinusoidal signal generator, connecting successive electrodes to signals of relative phase 0°, 90°, 180°

and 270°, and then repeating the cycle across the whole array 22. As is well-known, such an array generates travelling wave DEP conditions.

The cell is illuminated by the light source 30 and is viewed on the screen 36. In transmission, particles will be seen as distinct areas, and their movement can be clearly seen on the screen.

All of the multi-phased signals of the two or three different frequencies are electrically summed to each other in the required phase and then applied to the electrode array 22.

The electrodes may be of any form in order to apply the desired TWD field. The electrodes may be formed on one or more substrates, on the inner or outer walls of a dielectrophoresis cell, or on opposite faces of a dielectrophoresis cell. The electrode arrays may be in the form of wires which pass between substrates. The TWD electrode arrays of three or more electrodes may be used in conjunction with an additional electrode or electrode array to apply static DEP or electrostatic forces. The two sets of electrodes may be mounted in same plane, or mounted in such a way that the static DEP or electrostatic forces generated are in a different plane to that of the travelling field. Further additional forces may be applied in conjunction with the TWD field, such as fluid flow, optical, magnetic, gravity, including mechanical or physical movement of the dielectrophoretic cell, or any other force which may aid a separation or characterisation of one or more particles.

In a further example, two TWD arrays can be mounted at an angle to each other. The same or different frequencies may be applied to these arrays. Where

different frequencies are applied, they may be chosen such that they excite different parts of the dielectrophoresis spectrum. Different particles will thus be affected differently, and as differing forces are applied at differing angles relative to each other, differing particles will travel in differing directions and at different angles relative to a reference point. The angle at which the particle travels will be the result of the combined forces. This allows for extremely sensitive characterisation or separation of particles, with the particles being manipulated by intersecting travelling fields.

To further aid with particle separation, and means of a further example, the particles themselves may be altered by means such as: the stressing or damaging of one or more particle types, for example the lysing or stressing of red blood cells; the varying of the temperature to selectively stress particles; chemical agents or proteins added to the solution; conductivity, permittivity, pH, or other physiological content of the suspending medium altered; additional particles attached to the mentioned particles. All of these allow for increased differentiation of particles by altering their dielectrophoresis spectra, allowing improved characterisation, manipulation and/or detection by means of the invention.

An example will now be given of the practical application of widening a TWD window as described with reference to Figures 2 and 3.

At present, without use of the inventive arrangement, TWD can only be utilised over a relatively narrow frequency region or window of the complete spectrum. A dielectrophoresis spectrum for a particular particle can be considered as having a number of different regions

corresponding to particular properties of the particle. Different particles exhibit different dielectrophoresis spectra and it is therefore clearly of benefit to extend the frequency range over which TWD may be undertaken.

As an example, experiments were completed on human whole blood. The whole blood was diluted 20 times in buffer solution of 5% mannitol with a conductivity of 200 μS/cm and an approximate cell concentration of 2.5 x 10^8 cells per ml. The experiments were completed with an array of serpentine TWD electrodes (as disclosed in our co-pending Application ? filed on even date). The electrodes were sinusoidal in shape with electrode width 8 μm and inter-electrode gap of 17 μm in the central channel region - the main region of cell movement. A second frequency signal of four volts peak-to-peak at 55 kHz was applied. This signal was a static DEP signal. A TWD signal was applied at a frequency of 55 kHz. With the addition of the second frequency signal, TWD was observable over the frequency range 10 kHz to 18 MHz. The peak of the travelling speed, and thus the negative peak of the imaginary spectrum, was found to be around 250 kHz. The crossover frequency of the imaginary spectrum (i.e. where I = 0) was found to be around 5 MHz, and for a narrow frequency range centred on this value, there was no TWD movement. The frequency range over which reliable TWD was possible with a single frequency was 10 kHz up to 150 kHz. The addition of a second frequency thus extended the TWD window considerably, allowing TWD to be performed over most of the complete dielectrophoretic spectrum.

It should be noted here that the electrophoresis spectrum is quite different at the conductivity of 200 μS/cm to the spectra shown in Figures 1 and 2. The crossover frequency, etc. is significantly different, although the general shape of the spectrum is similar.

For reference, the dielectrophoresis spectrum expected for human red blood cells at suspending medium conductivity 200 μS/cm is shown in Figure 10. As in Figure 1, the real part of the dielectrophoretic force is labelled R and the imaginary part I. The frequency range over which TWD was completed (10 kHz up to 18 MHz) with the addition of a second signal at frequency 55 kHz indicated by the arrow TW. The spectrum in Figure 10 is an unmodified spectrum, in that the effect of applying the second frequency is not shown, although its position as indicated at F10.

By application of the inventive technique of applying a TWD force and a second signal at a frequency which modifies the TWD force, several advantageous results can be achieved, including:

a) separation of cells to high specificity for identification and enumeration;

b) separation of rare target cells from heterogenous samples, avoiding cell loss with a process that uses only one procedure;

c) processing of samples at high cell sorting rates;

d) separation of cells without the need for biochemical labelling or modification;

e) isolation of viable, culturable cells with little or no biological damage.

CLAIMS

1. A method of travelling wave dielectrophoresis comprises applying to a suspension of particles a first signal at a first frequency and at a plurality of different phases whereby the particles experience a travelling wave dielectrophoretic force, and simultaneously applying a second signal at a second frequency whereby either the real part or the imaginary part of the travelling wave dielectrophoretic force on the particles at the first frequency is altered in magnitude.

2. A method according to Claim 1 whereby within a range of first frequencies, the particles experience a travelling wave dielectrophoretic force of which there is a real part which is negative and of which there is also an imaginary part, said range of first frequencies constituting a travelling wave dielectrophoretic window, and applying the second signal whereby the window is varied in width.

3. A method according to Claim 1 in which the frequency of the second signal is selected so that the levitation height of the particles above the electrodes applying the signals is varied.

4. A method according to any one of Claims 1 to 3 in which there are two types of particle in suspension, and the second frequency is selected so that the speed of travel of at least one particle type is varied.

5. A method according to Claim 4 in which the second frequency is selected so that the relative speed of travel of the two particle types is increased.

6. A method according to Claim 5 in which one particle

type travels and the other does not.

7. A method according to Claim 4 in which the second frequency is selected so that the relative speed of travel of the two particle types is decreased.

8. A method according to Claim 4 in which the second frequency is selected so that both types of particle travel at the same time.

9. A method according to Claim 4 in which the second frequency is selected so that the two types of particle travel in opposite directions.

10. A method according to any one of Claims 1 to 9 in which the second signal generates a static DEP field.

11. A method according to any one of Claims 1 to 9 in which the second signal generates a second travelling wave dielectrophoretic field.

12. A method according to Claim 11 in which the first and second travelling wave signals are arranged reverse phase.

13. A method according to Claim 1 in which the second signal is applied at a frequency at which one of said real part and said imaginary part is zero and the other part is positive, so that said other part increases in value in accordance with the strength of the second signal.

14. A method according to Claim 1 in which the second signal is applied at a frequency at which one of said real part and said imaginary part of the force is zero and the other part is negative, so that said other part decreases in value in accordance with the strength of

the second signal.

15. A method according to any preceding Claim further comprising applying a third signal at a third frequency whereby either the real part or the imaginary part of the travelling wave dielectrophoretic force on the particles is altered in magnitude.

16. A method of separating unwanted particles from body fluid particles comprises applying to a suspension of both types of particle in a liquid a TWD field at a first frequency, and simultaneously applying a second electrical field at a second frequency, whereby the speed or direction of travel in the TWD field of one particle type is altered.

17. A method according to Claim 16 in which the unwanted particles are cancer cells and the body fluid particles are blood cells.

18. A method according to Claim 16 in which the unwanted particles are bacteria and the body fluid particles are blood cells.

19. A method according to Claim 18 in which the bacteria are E-coli and the blood cells are red blood cells, the first and second frequencies being selected so that E-coli travels in the TWD field and the red blood cells do not travel.

20. A method according to Claim 18 in which the bacteria are E-coli and the blood cells are red blood cells, further comprising applying a third electrical signal at a third frequency, the first, second and third frequencies being selected so that E-coli travels in one direction in the TWD field and the red blood cells travel in the opposite direction.

21. A method according to any preceding Claim in which the second signal is selected to induce a hydrodynamic fluid movement of said suspension.

22. A method of applying TWD to human blood cells comprises applying to a suspension of said cells, as first TWD, signal at a frequency of 55 kHz and a second, static DEP signal at a frequency of 55 kHz, whereby the TWD window extends between 10 kHz and 18 MHz.

23. Apparatus for the application of travelling wave dielectrophoresis comprising an electrode array on a substrate, means to apply to the array a first signal at a first frequency and a plurality of different phases and simultaneously to apply a second signal at a second frequency.

24. Apparatus according to Claim 23 in which the second signal is applied at the same plurality of phases as the first signal.

25. Apparatus according to Claim 23 in which the second signal is applied at a single phase.

26. Apparatus according to any one of Claims 23, 24 and 25 in which the substrate is transparent and further comprising illumination means to illuminate the substrate and viewing means to view any particles on the substrate.

27. Apparatus for the application of travelling wave dielectrophoresis as hereinbefore described with reference to Figure 9 of the accompanying drawings.

ABSTRACT

TRAVELLING WAVE DIELECTROPHORETIC APPARATUS AND METHOD

A method of travelling wave dielectrophoresis applicable to a suspension of particles in which a first signal at a first frequency and a plurality of different phases is applied to generate a TWD force, and simultaneously a second signal is applied at a second frequency which alters the real or the imaginary part of the TWD force on the particles at the first frequency. Either the travelling wave window is varied in width, or the levitation height of the particles is varied. When there are two types of particle present, the speed of particle travel may be varied so that one type travels and the other does not, or the types travel in opposite directions to assist particle separation.

Fig. 3

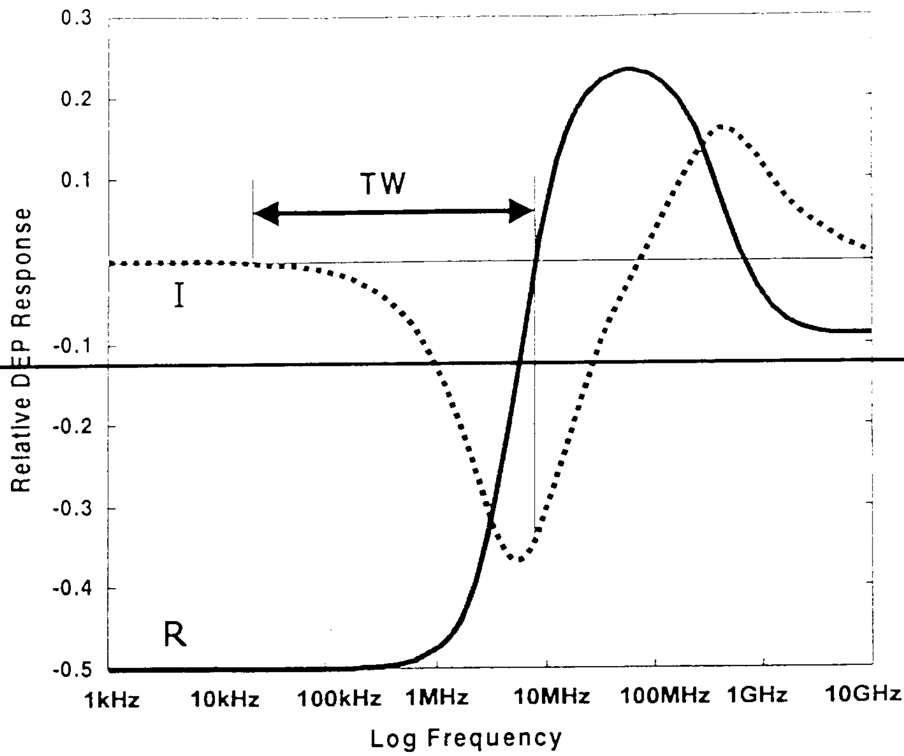

0.3
0.2
0.1
-0.1
-0.2
-0.3
-0.4
-0.5
TW
I
R
Relative DEP Response
1kHz
10kHz
100kHz
1MHz
10MHz
100MHz
1GHz
10GHz
Log Frequency

Fig. 1

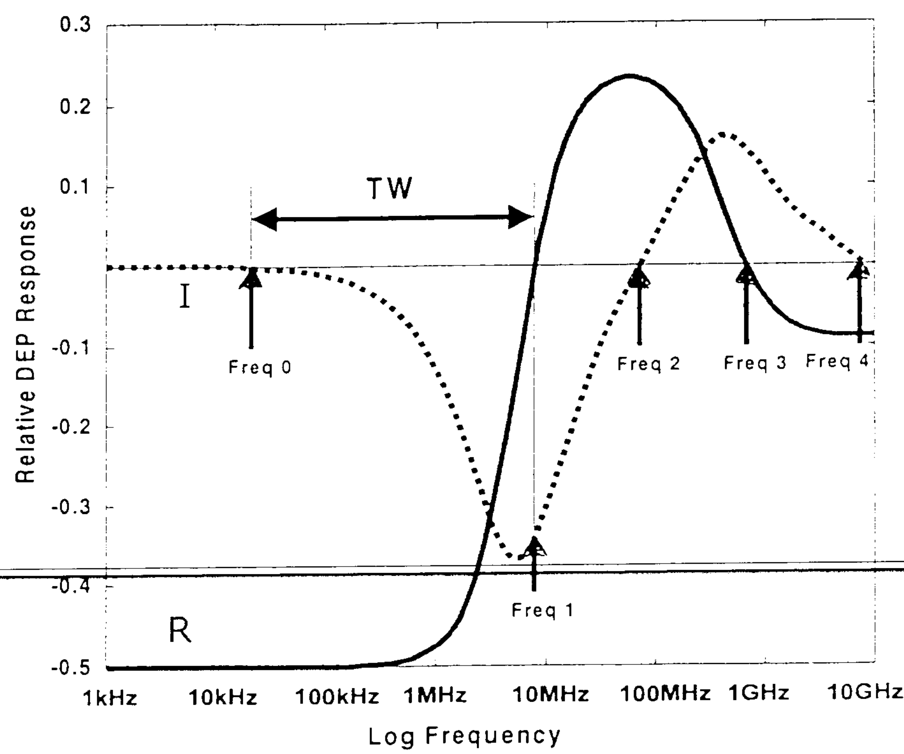

0.3
0.2
0.1
-0.1
-0.2
-0.3
-0.4
-0.5
TW
I
R
Freq 0
Freq 1
Freq 2
Freq 3
Freq 4
Relative DEP Response
1kHz
10kHz
100kHz
1MHz
10MHz
100MHz
1GHz
10GHz
Log Frequency

Fig. 2

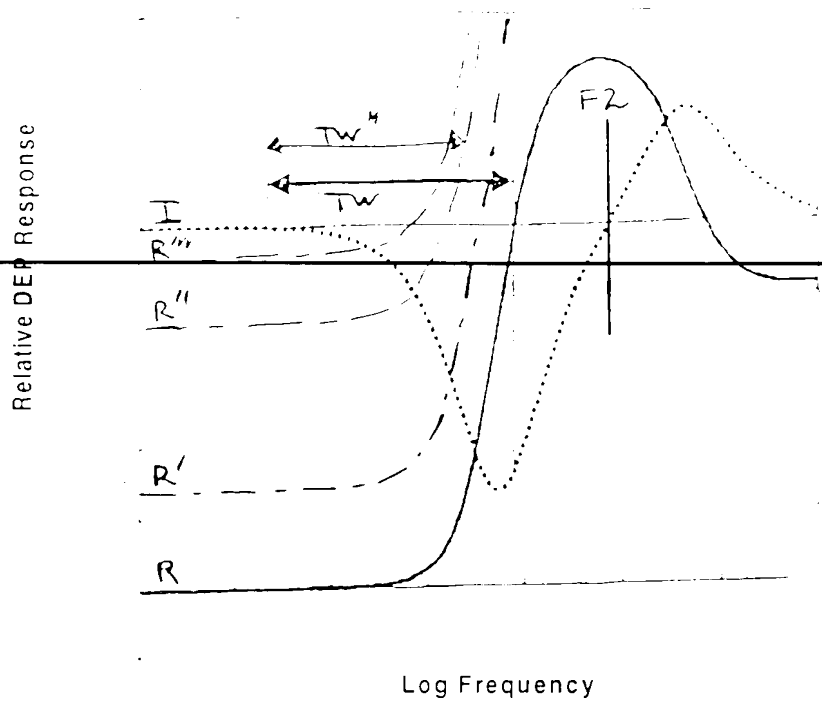

Relative DEP Response
Log Frequency
F2
TW"
TW
I
R'''
R''
R'
R

Fig. 3

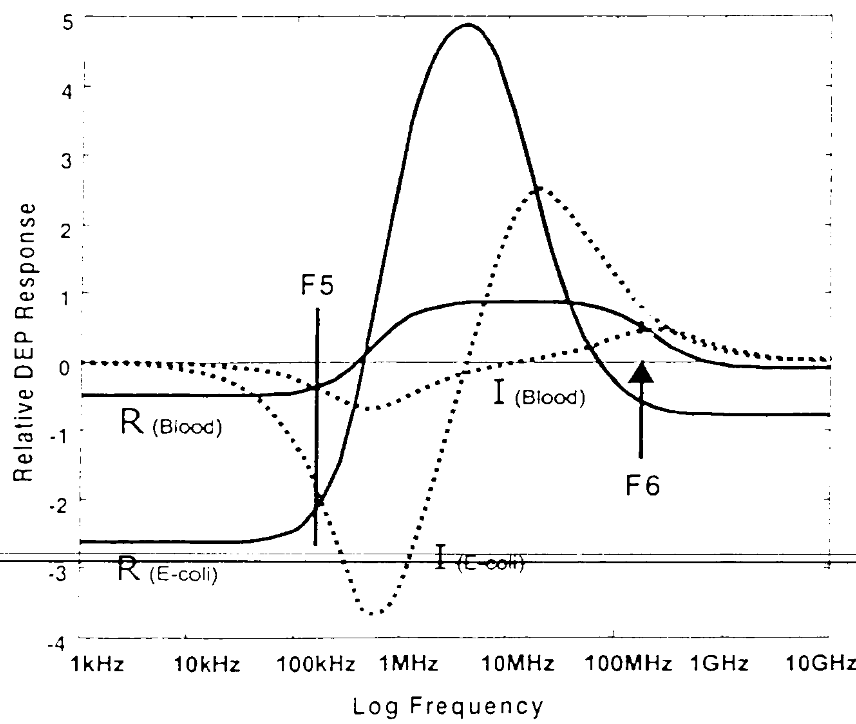
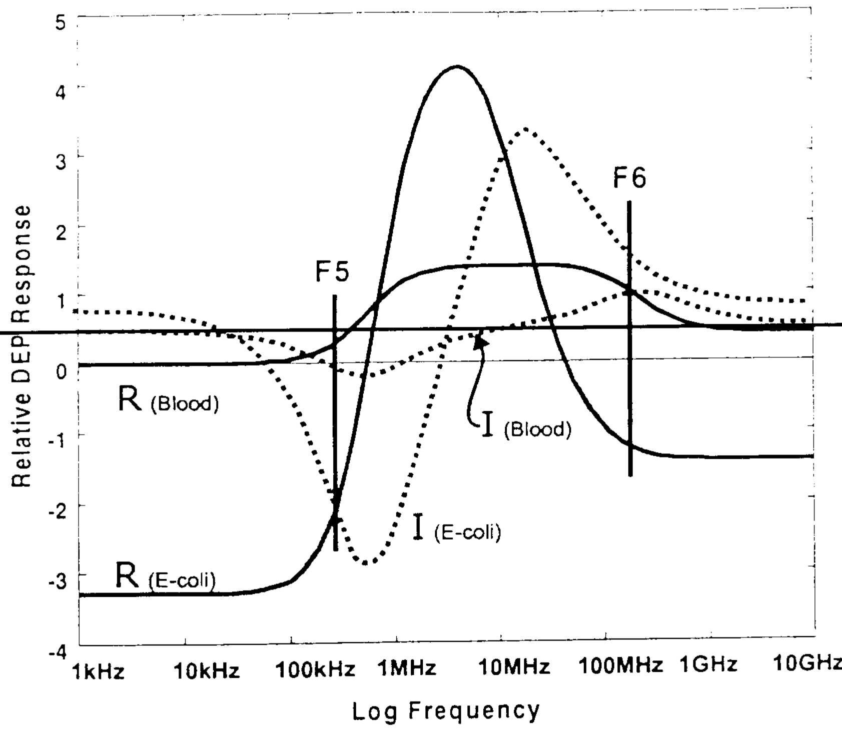
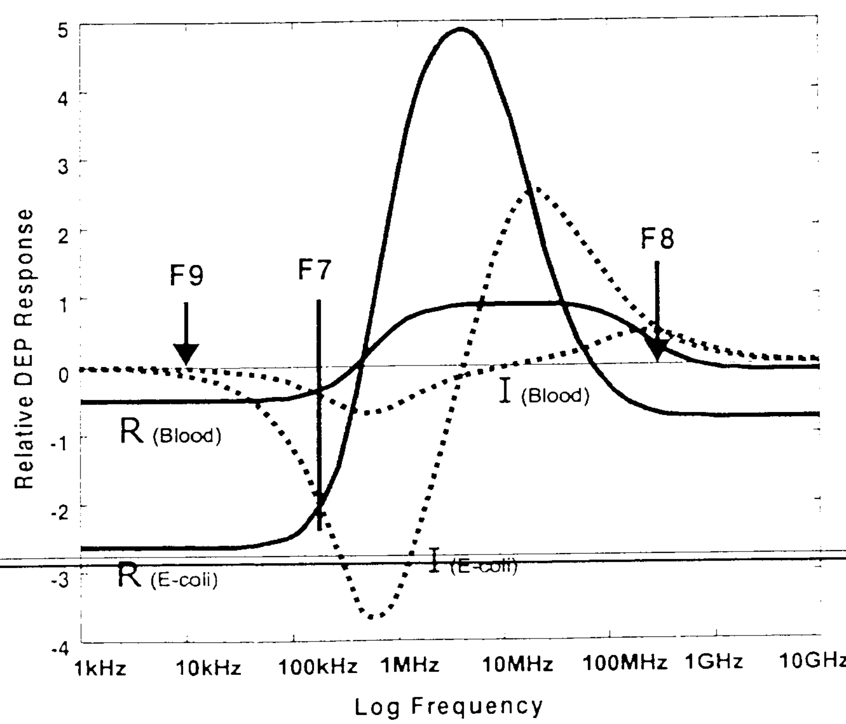

Relative DEP Response
5
4
3
2
1
0
-1
-2
-3
-4
F5
F6
R (Blood)
I (Blood)
R (E-coli)
I (E-coli)
1kHz
10kHz
100kHz
1MHz
10MHz
100MHz
1GHz
10GHz
Log Frequency

Fig. 4



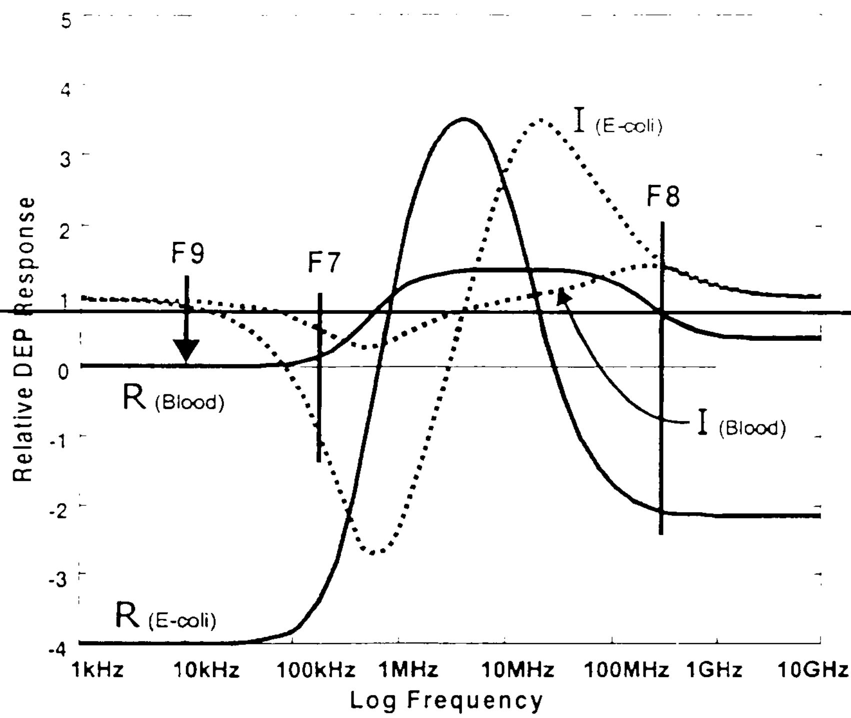
Relative DEP Response
Log Frequency
1kHz
10kHz
100kHz
1MHz
10MHz
100MHz
1GHz
10GHz
F5
F6
R (Blood)
R (E-coli)
I (Blood)
I (E-coli)

Fig. 5



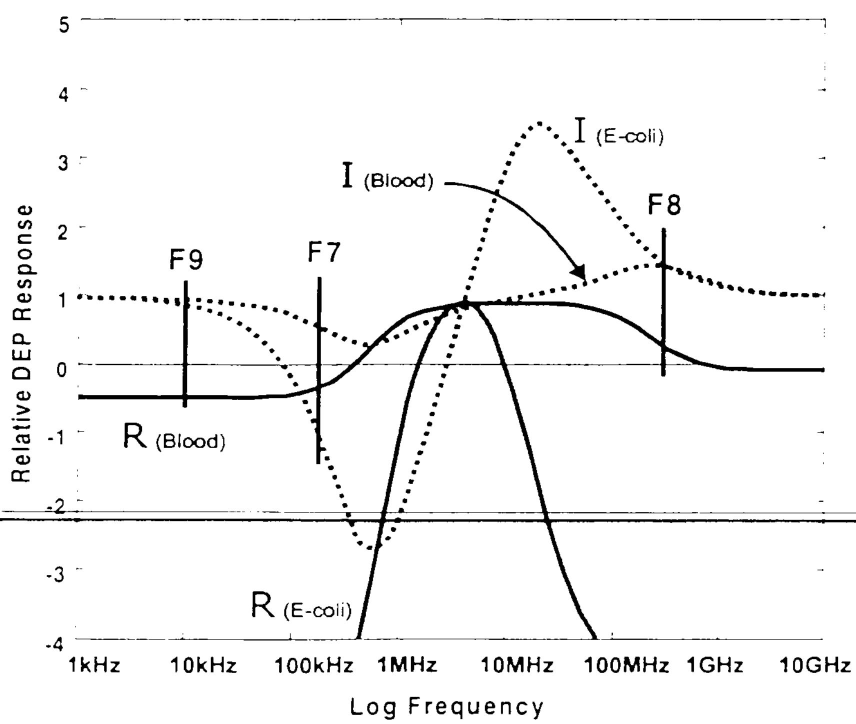
Relative DEP Response
Log Frequency
1kHz
10kHz
100kHz
1MHz
10MHz
100MHz
1GHz
10GHz
F9
F7
F8
R (Blood)
R (E-coli)
I (Blood)
I (E-coli)

Fig. 6



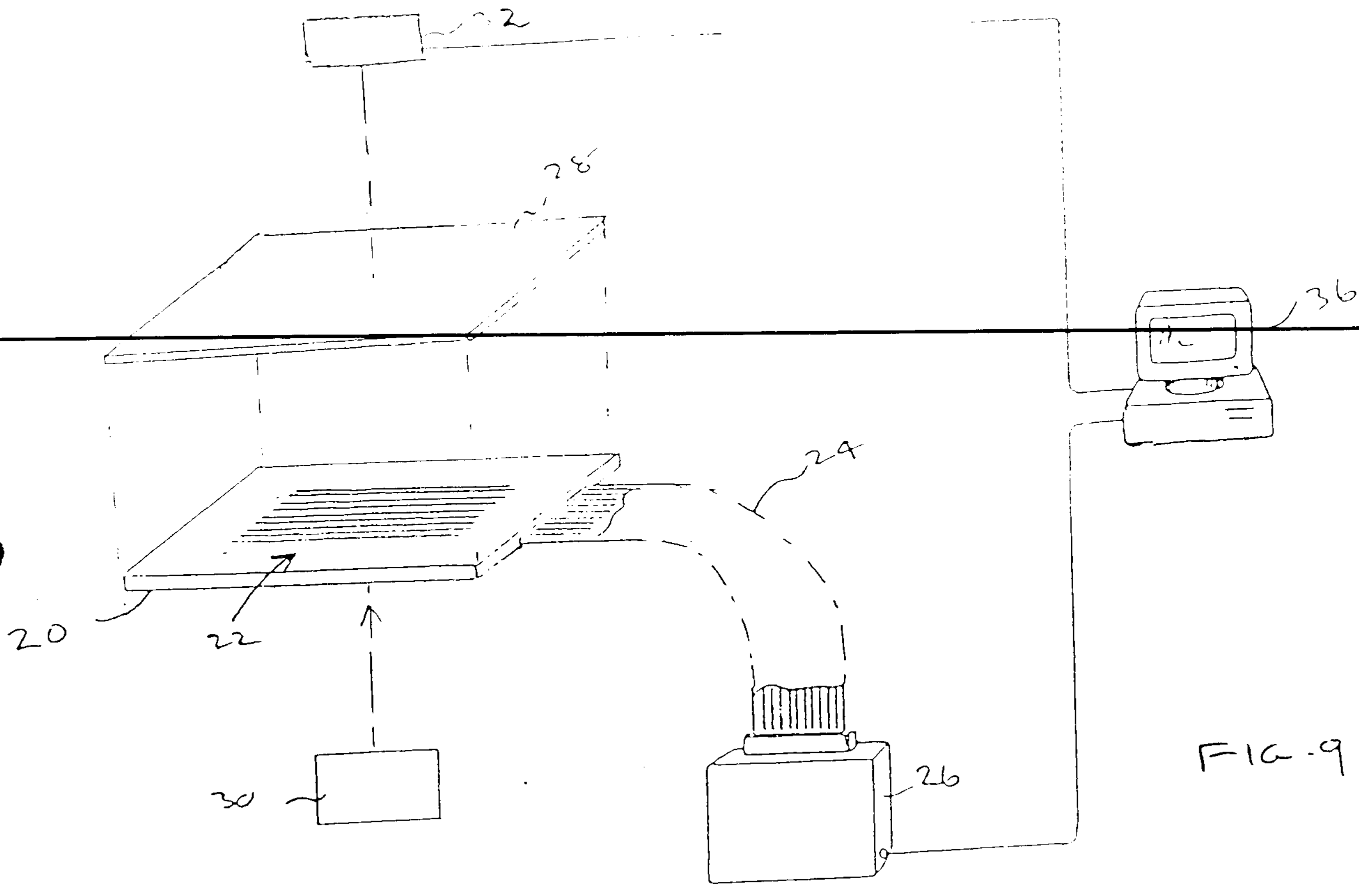
5
4
3
2
1
0
-1
-2
-3
-4
Relative DEP Response
I (E-coli)
F8
F9
F7
R (Blood)
I (Blood)
R (E-coli)
1kHz
10kHz
100kHz
1MHz
10MHz
100MHz
1GHz
10GHz
Log Frequency

Fig. 7



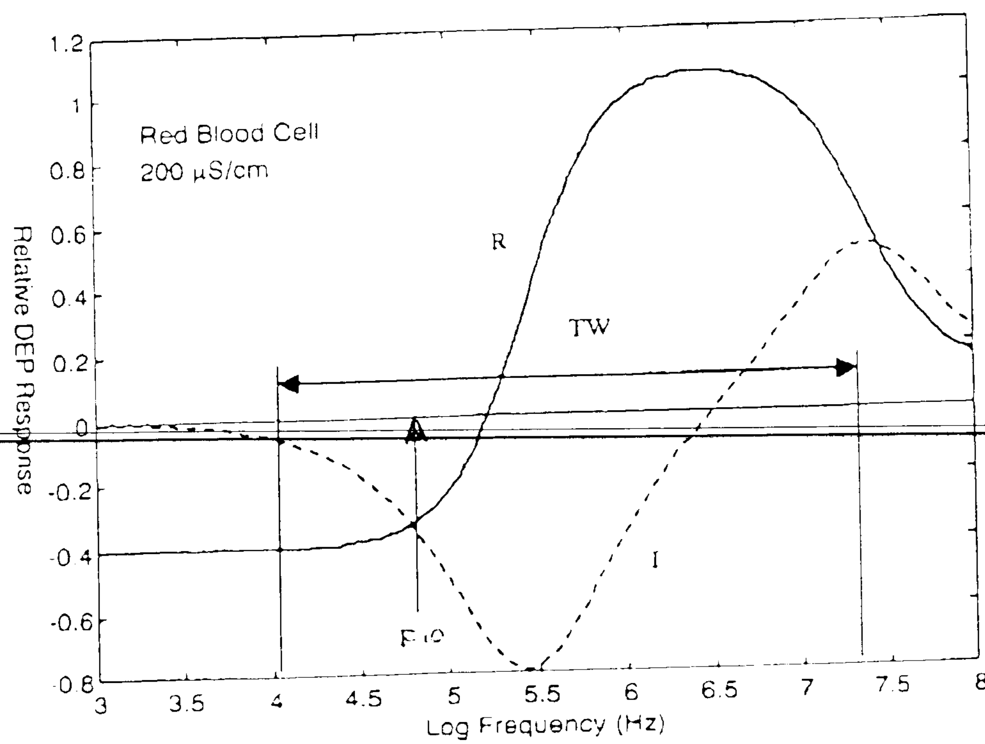
5
4
3
2
1
0
-1
-2
-3
-4
Relative DEP Response
I (E-coli)
I (Blood)
F8
F9
F7
R (Blood)
R (E-coli)
1kHz
10kHz
100kHz
1MHz
10MHz
100MHz
1GHz
10GHz
Log Frequency

Fig. 8



32
28
36
24
20
22
30
26

FIG. 9



Red Blood Cell
200 μS/cm
R
TW
I
Relative DEP Response
Log Frequency (Hz)
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
3
3.5
4
4.5
5
5.5
6
6.5
7
7.5
8

FIG. 10